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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/829,404	04/20/2004	Colin Henry Self	44008-010200	5958

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EXAMINER	
HUMPHREY, DAVID HAROLD	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 04/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/829,404	SELF, COLIN HENRY	
	Examiner	Art Unit	
	David Humphrey	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 17-24 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 17-24 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/945,868.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-9 are canceled by the Applicants amendment received on 04/20/2004.

Claims 17-24 are added.

Claims 17-24 are pending.

Claims 17-24 are examined on the merits.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The oath cites the incorrect application number for foreign priority under 35 U.S.C. 119. The prior foreign application listed should be PCT/GB96/01066 and not PCT/GB/010966.

Specification

3. Applicant is required to state the status (pending, allowed, etc.) of all parent priority applications in the first line of the specification. The status of all citations of US filed applications in the specification should also be updated where appropriate.

Claim objections

4. Claims 17-24 are objected to because of the following informalities: the text of any claims added by amendment must not be underlined. See MPEP § 714 (page 700-218, left column, lines 11-13, Rev. 3, August 2005). Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 17-24 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 17 is vague and indefinite for the recitation of analyzing a mixture. It is unclear what components are in the mixture. The mixture could include a mixture of cell types, protein-containing cell lysates, blood or body fluid samples, etc. Accordingly, one of ordinary skill in the art would be unable to determine the metes and bounds of the claimed invention.

b. Claim 17 is vague and indefinite for the recitation, "an analyte which is a member of a binding pair". It is unclear whether the other member of the binding pair is an antibody, a macromolecule, or some other unidentified molecule.

c. Claim 17 is vague and indefinite for the recitation, "assaying the macromolecule for the presence of the analyte". It is unclear how the macromolecule

and the analyte come into contact. It is also unclear how assaying the macromolecule provides information on the presence of the analyte. Applicant is requested to clarify.

d. Claim 17 recites the limitation "the capability" in line 4 and in line 7. There is insufficient antecedent basis for this limitation in the claim.

e. Claim 17 recites the limitation "the inhibited antibody" in line 5. There is insufficient antecedent basis for this limitation in the claim.

f. Claim 18 is vague and indefinite for the recitation of "a first antibody component capable of binding a receptor". It is unclear what receptor is being referred to.

g. Claim 19 is vague and indefinite for the recitation, "parts of antibodies which retain the active site". It is unclear why the term "active site" which is commonly used to refer to the binding site of substrates for enzymes is used in this instant case, unless the antibodies are catalytic. Therefore, the metes and bounds of the claim cannot be determined. Applicant is requested to clarify.

h. Claim 19 recites the limitation "the active site" in line 2. There is insufficient antecedent basis for this limitation in the claim.

i. Claim 20 is vague and indefinite for the recitation of "the second antibody component is *against* an enzyme". It is unclear how the antibody component is opposed to the enzyme. It is not clear if the Applicant intended for the claim to read on the antibody binds to an enzyme. Applicant is requested to clarify.

j. Claims 23 and 24 recite the limitation "the electromagnetic radiation". There is insufficient antecedent basis for this limitation in the claim. Claim 17, upon which claims 23 and 24 depend, recite electromagnetic energy not electromagnetic radiation.

Clarification and/or correction are required.

Claim Rejections - 35 USC § 112, first paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 17-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir,1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue' not 'experimentation'. " (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the

claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided by the inventor, (7) the existence of working examples, (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims and the nature of the invention: The claims are drawn to a method of analyzing a mixture to determine the presence of an analyte, the method comprising providing an antibody that can bind both an analyte and a macromolecule. The antibody is reversibly inhibited from binding the macromolecule by the presence of a photocleavabe moiety until the mixture is exposed to electromagnetic energy to activate the capability of the antibody to bind the macromolecule. The macromolecule is then assayed for the presence of the analyte. Claims 18 and 19 recite the method wherein the antibodies can be bispecific antibodies or portions of antibodies that retain their bindings sites but are free of the Fc regions. Claims 20 and 21 are drawn to the method wherein the second antibody component can binds an enzyme, which converts a pro-drug into a cytotoxic drug. Claim 22 recites that method wherein the photocleavable moiety is –nitrophenylethan-1-ol conjugated to the antibody. Claims 23 and 24 recite the method wherein the electromagnetic energy is selected from the group consisting of ultraviolet, visible light, x-rays, and UV-A radiation.

Therefore, the claims encompass a method to analyze *any* mixture to determine the presence of *any* analyte, by providing an antibody that binds simultaneously to *any* analyte and *any* macromolecule including *any* enzyme, wherein the binding of the

antibody to the macromolecule is reversibly inhibited by the presence of a photocleavable moiety. Thus, the claims are very broad and encompass methods of using unspecified mixtures, macromolecules, and antibodies to determine the presence of any analytes.

The amount of direction provided by the inventor and the existence of working examples: Applicants' specification cites several examples. However, none seem to specifically recite the claimed invention. The claimed invention appears to be a method of analyzing for the presence of CEA on tumor cells. This method appears to comprise the implementation of a bispecific antibody, which should bind the CEA antigen analyte, as well as an alkaline phosphatase enzyme macromolecule when not inhibited by NPE. Once the inhibition of the bispecific antibody to alkaline phosphatase is reversed the said antibody should be able to bind the alkaline phosphatase and consequently able to assay the presence for the CEA. Applicant's claims or specification do no clearly and specifically recite what the Examiner assumes is the claimed invention. For example, Example 1, on page 21, discloses only how to make an antibody that binds to CEA and reversibly binds to alkaline phosphatase. Example 2 does not identify what antibody is used, whether or not alkaline phosphatase is added, and what analyte is analyzed on the human carcinoma cell line. On page 23, Examples 3-5 present various methods for producing antibodies or antibody fragments that have been established by others. Examples 1A, 2A, 3B, and 5A, comprise irradiating the bispecific antibodies before adding them to the cells. These examples are not commensurate in scope with the claims which recite mixing the inhibited antibody with a mixture prior to exposing the

mixture to electromagnetic energy. Example 3A discloses a method wherein the mixture is irradiated after the antibodies have been added. However, irradiation time vs. visual color does not provide evidence that more enzyme is being activated. Although, Applicants have described that there are roughly 8-12 NPE residues per antibody molecule (see page 24, lines 8-10) that does preclude that some antibodies do not contain any NPE. This is evidenced by the initial color seen without any irradiation for the 5.0 micrograms/ml measurement. If enzyme activity already exists in the sample, it is unclear to what extent the activated antibody-enzyme conjugate contributes to the overall assay. In addition, if this example was truly demonstrated activation of an antibody-enzyme complex, the rate of reaction for the 5.0 micrograms/ml reaction should be 2x that of the 2.5 micrograms/ml sample, which it is clearly not. In fact, one could argue that the rate of reaction for the 2.5 micrograms/ml sample is faster. The specification does not provide guidance commensurate in scope with the claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed inventions without undue experimentation. In re Wright, 27 USPQ2d 1510 (CAFC). The disclosure does not demonstrate sufficient evidence to support Applicants' claim to a method of analyzing a mixture using an antibody capable of binding an analyte and a macromolecule which the capability of binding to the macromolecule is reversibly inhibited, exposing the mixture to electromagnetic energy to allow the macromolecule to bind, and assaying the macromolecule for the presence of the

analyte. All of the factors considered in the sections above, underscores the criticality of providing working examples in the specification for an unpredictable art such as providing gene therapy to animals to treating cardiovascular diseases.

Quantity of experimentation needed to make or use the invention based on the content of the disclosure: In view of the Wands factors considered above, one of ordinary skill in the art would conclude that a method of analyzing a mixture to determine the presence of an analyte would require undue experimentation in order to use the invention as claimed by the Applicants.

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Humphrey whose telephone number is (571) 272-5544. The examiner can normally be reached on Mon-Fri 8:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

David Humphrey, Ph.D.

April 2, 2006